Supplementary Material:

A Kinetic Study of Domain Swapping in Protein L

For a homodimerization reaction of a protein according to the scheme

$$M + M \underset{k_{mon}}{\overset{k_{dim}}{\rightleftharpoons}} D$$

k_{dim} and k_{mon} are the rate constants for dimerization and monomerization, and the dissociation constant of the homodimer D is given by

(1) $$K_d = \frac{k_{mon}}{k_{dim}}$$

The rate equations for the forward and backward reactions are:

(2) $$\frac{d[M]}{dt} = -k_{dim}[M]^2 + 2k_{mon}[D]$$

(3) $$\frac{d[D]}{dt} = k_{dim}[M]^2 - k_{mon}[D]$$

where [M] and [D] are the concentrations of the momomeric and the dimeric state.

For a total concentration of protein, c_0, with

(4) $$c_0 = [M] + 2 \cdot [D]$$

[M] is given by

(5) $$[M] = c_0 - 2 \cdot [D]$$

Using equations (1) and (5) the rate equation (3) can be recast to

(6) $$\frac{d[\mathrm{D}]}{dt} = k_{dim}\left(c_0 - 2\cdot[\mathrm{D}]\right)^2 - k_{\mathrm{dim}}\cdot K_d\cdot[\mathrm{D}]$$

which can be written as

(7) $$\frac{d[\mathrm{D}]}{-\left([\mathrm{D}]^2 + [D]\cdot(-c_0 - \frac{K_d}{4}) + \frac{1}{4}(c_0)^2\right)} = -4k_{dim}dt$$

expansion of the left hand side into partial fractions using

(8) $$\frac{d[\mathrm{D}]}{-\left([\mathrm{D}] - \lambda_1\right)\cdot\left([\mathrm{D}] - \lambda_2\right)} = -4k_{dim}dt$$

and

(9) $$\lambda_{1/2} = \frac{1}{2}\left(\frac{k_{mon}}{4k_{dim}} + c_0\right) \pm \sqrt{\frac{1}{4}\left(\frac{k_{mon}}{4k_{dim}} + c_0\right)^2 - \frac{1}{4}\left(c_0\right)^2}$$

yields

(10) $$-\frac{d[\mathrm{D}]}{\left(\lambda_1 - \lambda_2\right)\left([\mathrm{D}] - \lambda_1\right)} + \frac{d[\mathrm{D}]}{\left(\lambda_1 - \lambda_2\right)\left([\mathrm{D}] - \lambda_2\right)} = -4k_{dim}dt$$

Integration of equation (10) on both sides gives

(11) $$\frac{1}{\left(\lambda_1 - \lambda_2\right)}\cdot\ln\left(\frac{[\mathrm{D}] - \lambda_2}{[\mathrm{D}] - \lambda_1}\right) = -4k_{dim}t + const$$

Assuming [D] = 0 at $t = 0$ (*i.e.* starting the reaction from the monomer) to calculate

$$(12) \qquad const = \frac{1}{(\lambda_1 - \lambda_2)} \cdot \ln\left(\frac{\lambda_2}{\lambda_1}\right)$$

yields the time course of the concentrations of homodimer, [D(t)], and monomer, [M(t)], as

$$(13) \qquad [D(t)] = \frac{\lambda_1 \lambda_2 \left(1 - \exp\left(-4k_{dim}(\lambda_1 - \lambda_2) \cdot t\right)\right)}{\lambda_1 - \lambda_2 \exp\left(-4k_{dim}(\lambda_1 - \lambda_2) \cdot t\right)}$$

$$(14) \qquad [M(t)] = c_0 - 2\frac{\lambda_1 \lambda_2 \left(1 - \exp\left(-4k_{dim}(\lambda_1 - \lambda_2) \cdot t\right)\right)}{\lambda_1 - \lambda_2 \exp\left(-4k_{dim}(\lambda_1 - \lambda_2) \cdot t\right)}$$

Populations of M and D are obtained by dividing equations (13) and (14) by c_0.